REMARKS

Claims 1, 23, 24 and 26 have been amended. Claims 1 and 23-32 remain in the application. Reexamination and reconsideration of the application as amended is requested.

The Examiner has provisionally rejected claims 1 and 23-22 under the doctrine of obviousness double patenting. By means of the undersigned, Applicant herewith files a terminal disclaimer in compliance with 37 CFR 1.321(c) to limit the term of the patent issuing from the current application to the term of U.S. Patent No. 5,728,541, issuing from U.S. Patent Application Serial No. 08/679,056, and any patent issuing from U.S. Patent Application Serial No. 09/095,993. Besides these, there are no other related pending applications.

The Examiner has rejected claims 23-32 under 35 U.S.C. § 102 (b) for purported anticipation by each of U.S. Patent No. 5,242,806 to Yen-Maguire et al., U.S. Patent No. 4,423,145 to Stampfer et al., U.S. Patent No. 5,270,172 to Morgan and U.S. Patent No. 4,937,187 to Rotman. The examiner asserts that the claims are written in open-ended "comprising" terminology which does not exclude disaggregating the specimen (i.e., reducing it to individual cells). However, though claim 23 contains the "comprising" transitional expression, part b) of the claim refers to "avoidance of further size reduction of the particles thereafter." Because of the use of this terminology, the claim does not read on disaggregation. For these reasons, it is believed that the rejection has been overcome.

The Examiner has requested that a list be provided that specifically points out written description in the specification as filed for each of the features of new claims 25-32. The list follows:

Claim	Feature	Written Description
25	Plasminogen Activator Inhibitors Type 1 (PAI-1)	p. 2, lines 25-26 p. 13, line 24
25	Eurokinase-Type Plasminogen Activator (u-PA)	p. 2, lines 24-25 p. 13, line 24
25	α-fetoprotein	p. 2, line 32
25	Carcinembryonic Antigen	p. 2, line 32 p. 13, line 25
25	Transforming Growth Factor α	p. 2, lines 32-33
25	Transforming Growth Factor β	p. 2, lines 32-33
25	Major Histocompatibility Complex (MHC) Molecules	p. 14, line 6
26	Wound Healing Agent	p. 6, line 19
27	Radiation Therapy	Example 1, p. 14, line 15 ff.
27	Radiation Therapy Sensitizing Or Ameliorating Agent	p. 6, lines 13-14
28	Immunotherapeutic Agent	p. 6, lines 14-15 Example 2, p. 16, line 1 ff.
29	Sampling a quantity of medium from the tissue culture monolayer of step c) to identify the presence or absence of cellular markers, secreted factors or tumor antigens indicative of a disease state	p. 13, lines 15-37
30	Gene Therapy Agent	Example 3, p. 17, line 27 ff.
31	Antisense Oligonucleotide Gene Therapy Agent	Example 3, p. 17, line 27 ff.
32	Combination Of Two Or More Therapeutic Agents	Example 4, p. 19, line 19 ff.

The Examiner has rejected claims 1 and 23-32 under 35 U.S.C. § 112, first paragraph, for purported lack of support by the specification. The Examiner asserts that the newly added limitation directed to non-malignant cells and cells in general is not enabled. In response, independent claims 1 and 23 have been amended to refer to hyperproliferative cells. Support for this term is found on page 6, line 18 of the specification. Hyperproliferative disorders are understood in the art to be generic to malignancy. The term "hyperproliferative" is used in reference to warts, premalignant lesions such as actinic keratoses and benign as well as malignant tumors. An example of this usage is provided in U.S. Patent No. 5,610,185 to Stanwell et al.

The Examiner has rejected claims 1 and 23-32 under 35 U.S.C. § 112, second paragraph, for indefiniteness. The Examiner asserts that, in claim 1(e), the treating of sites with treating means is not related to chemosensitivity, no determining takes place before and after

treating, and does not understand the reference to correlating chemosensitivity. Applicant notes that claim 1(e) refers to "correlating chemosensitivity of the cells in said plurality of sites to said at least one treating means" and that it is the express purpose of the present invention as described in the claim to relate the treating means used to the observed chemosensitivity of the cells. In regard to "determining," Applicant notes that, though the specification refers to cell counting before and after the treating process, "determining" as claimed involves a comparison that makes use of the results of both counting procedures. Therefore, the determining can take place only after the "treating" step. In regard to "correlating chemosensitivity," the invention, as is stated in the specification, relates to screening and testing of active agents, including chemotherapeutic agents, to predict potential efficacy in individual patients in whom treatment with such agents is indicated. In the method of the present invention, some cells are exposed to active agents or treating means; others, in a control group, are not. Comparison of the cells exposed to treating means with the cells in the control group, allows a correlation to be made between the treating means and its effect on the cells exposed to it. The Examiner also asserts that what the control is or controls is not recited. The term "control" is used in the specification in the sense accepted in all fields of science, and refers here to a standard of comparison for checking the results of an experiment. The specification refers, on p. 11, lines 9-10, to the use of a control solution that does not contain the active agent.

The Examiner asserts that the preamble of claim 23 is directed to assessing chemosensitivity of cells but that the claim lacks any such step. Section f) of claim 23 has been amended to emphasize the direction of this claim to assessing chemosensitivity of cells. The Examiner has queried the use of the term "cells ascites" in claim 23 (a). In response, this term has been canceled without prejudice, as Applicant intends to make material represented by this term the subject of a continuing application. The Examiner asserts that "said cohesive" in claim

23 lacks antecedent basis. Claim 23 has been amended to conform this terminology with the antecedent terminology.

The Examiner asserts that the term "active agent" in claim 24 lacks antecedent basis. Claim 24 has been amended to refer to a "treating means"; this terminology is used in claim 23. The Examiner asserts that, in claim 24, how the assessment takes place is indefinite and it is not seen how one could determine optimal sensitivity to a single agent in the presence of many agents. Claim 24 is drawn to the "Combination Chemotherapy" example at p. 19, line 19 in the specification. The purpose of the experiment is not to determine optimal sensitivity to a single agent in the presence of many agents. The experiment is designed to find the optimal combination of concentrations of two or more agents. Claim 24 has been amended to provide clarification.

The Examiner asserts that the term "the process" in claim 26 lacks antecedent basis. Claim 26 has been amended to refer to "the method"; this terminology is used in claim 25.

For these reasons, the Examiner's objections have been overcome. Therefore, it is submitted that the claims are in condition for allowance. Reconsideration and withdrawal of the rejections is requested. Allowance of claims 1 and 23-32 is respectfully requested.

Respectfully submitted,

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MARKED UP AMENDED CLAIMS

1. (Thrice Amended) A method for assessing chemosensitivity of [non-malignant] hyperproliferative cells consisting essentially of the steps of:

a) harvesting a specimen of a patient's tissue or cells;

b) separating mechanically said specimen into cohesive multicellular particulates with a particle size distribution between about 0.25 mm^3 and about 1.5 mm^3;

c) growing a tissue culture monolayer from said cohesive multicellular particulates;

d) inoculating cells from said monolayer into a plurality of segregated sites; and

e) treating each of said plurality of segregated sites with [at least one] a treating means, determining cell number relative to at least one control, followed by correlating chemosensitivity of the cells in said plurality of sites to said at least one treating means.

23. (Amended) A method for assessing chemosensitivity of hyperproliferative patient cells comprising the steps of:

a) harvesting a specimen of a patient's tissue[,] or cells [ascites, or effusion fluid];

b) mechanically separating said specimen into cohesive multicellular particulates having a particle size distribution between about 0.25 and about 1.5 mm^3 with avoidance of further size reduction of the particles thereafter;

c) growing a tissue culture monolayer from said cohesive multicellular particulates;

d) inoculating cells from said monolayer into a plurality of segregated sites;

e) treating each of said plurality of sites with [at least one] a treating means, determining cell number relative to at least one control, followed by correlating the chemosensitivity of the cells in said plurality of sites to said [at least one] treating means in order to assess the chemosensitivity of the patient cells; and

f) assessing the chemosensitivity of the cells in said plurality of sites, at least one of which sites further constitutes a control site, for cellular markers, secreted factors, or tumor antigens.

24. (Amended) The method according to claim 23 wherein step e) further comprises:

e) treating said plurality of sites with a plurality of [active agents] treating means, each of said plurality of sites being treated with a unique combination of concentrations of said treating means over a length of time adequate to permit assessment of both initial cytotoxic effect and longer-term inhibitory effect of at least one of said plurality of [active agents] treating means.

26. (Amended) The [process] method according to claim 23 wherein said treating means is a wound healing agent.